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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,495	BANGE, FRANZ-CHRISTOPH	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19-28 and 31-51* is/are pending in the application.

4a) Of the above claim(s) *12-17 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,24,25,28, 36-44, and 46-51* is/are rejected.

7)☒ Claim(s) *2, 4, 9, 19-28,31,33,36,37,39,43, 46,47,50* is/are objected to.

8)☒ Claim(s) *1-17,19-28 and 31-51* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15September2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's Response to Restriction Requirement, received 16 July 2008, is acknowledged. Applicant elects, with traverse, Invention I, claims 1-11, 19-44, and 46-51, drawn to hybridization probe and method of use.

Applicant's traversal is on the grounds that the combination of the amplification of a region of the *narGHJI* nitrate reductase operon and detection of a polymorphism specific for *M. tuberculosis* in that region is the specific technical feature that links Groups I and II, and that the primers of Group II are used in amplifying the region of the *nar GHJI* for the detection of the polymorphism specific for *M. tuberculosis* using the probes in Group I.

The examiner has considered applicant's traversal, but does not find it persuasive because for the reasoning put forth in the original restriction explanation. The specific inventive concept of Invention I is the specific probe which detects *M. tuberculosis* specific polymorphism, and the amplification of the nucleic acid sequences can be performed by any primer pair

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 18, 29, and 30 have been canceled. Claims 1-17, 19-28, and 31-51 have been amended.

Claims 1-17, 19-28, and 31-51 are pending and under consideration. Claims 12-17 and 45 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

3. Claims 1-11, 19-28, 31-44, and 46-51 are under consideration.

Specification

4. The disclosure is objected to because of the following informalities:

The numbering of the English translation is: Specification, 1-23, claims 25-31, page 32, and an abstract. Is there to be a page 24? What is the meaning/placement of the page 32?

Abstract, the five instances of "microbacterial" should be "mycobacterial".

Page 1, lines 13 and 15, "industrialised" should be "industrialized"; line 24, "immunisation" should be "immunization".

Page 2, line 3, "recognise" should be "recognize"; line 11, "characterised" should be "characterized".

Page 3, lines 2 and 13, "hybridisation" should be "hybridization"; line 23, "M. tuberculosis" should be in italics.

Page 4, lines 10, 11, 17, 18, and 21, "hybridisation" should be "hybridization"; line 16, what is meant by "i.e. above *M. bovis*"; lines, 23 and 28, "M. tuberculosis" should be in italics.

Page 5, line 5, "(in" should be "in"; line 6, what is meant by "compare Fig. 1"; lines 17, 26, and 27, "hybridisation" should be "hybridization"; lines 24 and 29, "M. tuberculosis" should be in italics.

Page 6, lines 1, 4, 13, and 19, "hybridisation" should be "hybridization"; line 15, "M. tuberculosis" should be in italics.

Page 7, line 7, "*and*" should not be in italics; lines 14, 18, 23, 24, and 29, "hybridisation" should be "hybridization"; line 28, what is meant by "compare e.g. Heid et al".

Page 8, lines 2, 4, 15, 18, 19, 21, and 23, "hybridisation" should be "hybridization".

Page 9, line 13, "hybridisation" should be "hybridization"; line 16, what is meant by "compare above".

Page 11, line 2, insert a comma between "urine" and "faeces".

Page 12, line 7, what is meant by "compare above"; line 12, "hybridise" should be "hybridize"; line 29, "hybridisation" should be "hybridization".

Page 13, line 4, "nucleoside" should be "nucleotide"; lines 13, 17, 22, 26, and 30, "hybridisation" should be "hybridization"; lines 22, and 30, "hybridises" should be "hybridizes".

Page 14, lines 4, 8, 12, 16, 21, 22, 25, and 27, "hybridisation" should be "hybridization".

Page 15, lines 1, 10, 11, 19, and 26, "hybridisation" should be "hybridization".

Page 16, lines 3 and 17, "hybridisation" should be "hybridization"; line 24, "sequences No. 1 to 6" should be "SEQ ID NOs: 1 to 6".

Page 17, lines 4, 7, 10, 17, and 20, "hybridisation" should be "hybridization"; line 24, "M. tuberculosis" should be in italics.

Page 19, line 15, "optimised" should be "optimized".

Page 20, lines 5, 8, 23, 24, 26, and 28, "hybridisation" should be "hybridization"; line 7, "Polymerisation" should be "Polymerization".

Page 21, line 1, "denaturisation" should be "denaturization"; lines 2, 4, 7, 10, 11, 13, and 14, "hybridisation" should be "hybridization".

Appropriate correction is required.

Drawings

5. Figures 1-5 are objected to because the wording is in German.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if

only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Sequence Identifier Requirement

6. M.P.E.P. §2422.02, third paragraph, recites that "the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings."

Figure 1 contains sequences without the required sequence identifiers. Appropriate correction is required.

Claim Objections

1. Claim 2 is objected to because of the following informalities: the first instance of "PCR", "NASBA", "SDA", and "LCR" should be defined. Appropriate correction is required.

2. Claim 4 is objected to because of the following informality: line 3, "hybridisation" should be "hybridization".

3. Claim 9 is objected to because of the following informality: line 3, "hybridisation" should be "hybridization".

4. Claim 19 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

5. Claim 20 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

6. Claim 21 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

7. Claim 22 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

8. Claim 23 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

9. Claim 24 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

10. Claim 25 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

11. Claim 26 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

12. Claim 27 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

13. Claim 28 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

14. Claim 31 is objected to because of the following informality: line 9, each instance of "hybridisation" should be "hybridization".

15. Claim 33 is objected to because of the following informality: line 2, "hybridisation" should be "hybridization".

16. Claim 36 is objected to because of the following informalities: line 2, "*mycobacterium*" should be "*Mycobacterium*"; lines 9, 14, and 15, "hybridisation" should be "hybridization".

17. Claim 37 is objected to because of the following informality: line 1, "hybridisation" should be "hybridization".

18. Claim 39 is objected to because of the following informality: line 3, "hybridisation" should be "hybridization".

19. Claim 43 is objected to because of the following informality: line 3, "hybridisation" should be "hybridization".

20. Claim 46 is objected to because of the following informality: line 1, "hybridises" should be "hybridizes".

21. Claim 47 is objected to because of the following informality: line 1, "hybridises" should be "hybridizes".

22. Claim 50 is objected to because of the following informality: line 5, "hybridisation" should be "hybridization".

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a method for determining presence or absence of *M. tuberculosis* in a biological sample comprising: (a) amplifying a DNA "segment" from the biological sample, and (b) determining the presence or absence of the polymorphism specific for *M. tuberculosis* in position -215 in the 5' to 3' direction upstream of the translation start codon GTG of the *narGHJI* nitrate reductase operon, wherein the presence of the polymorphism indicates the presence of *M. tuberculosis* and the absence of the polymorphism indicates absence of *M. tuberculosis*.

The only requirement of the amplification in step one is the use of a primer pair "capable" of amplifying a "segment" of DNA which might include a region of SEQ ID NO:1 that encompasses position -215 in the 5' to 3' direction upstream of the translation start codon GTG of the *narGHJI* nitrate reductase operon. Thus, the primer pairs are not actually required to amplify the critical sequence. Because of this, at least one embodiment of the claim is utilization of said primers, but amplification of a *M. tuberculosis* sequence segment which may not include said position -215. In these examples, any probes would not detect said polymorphism even thought the sample DNA is from *M. tuberculosis*.

Therefore, a positive result, i.e., detection of the polymorphism, would indicate the presence of *M. tuberculosis* in said biological sample. However, a negative result, i.e., no detection of said polymorphism, would not indicate the absence of *M. tuberculosis*, but may be due to amplification of *M. tuberculosis* DNA segments in the biological sample which may not include the polymorphism. A sample determined by this method may be a false negative

because the sample may actually include *M. tuberculosis* DNA segments, just not segments including said polymorphism.

Thus, it is unclear how one determines if a negative result is a true negative for *M. tuberculosis* or is a false negative due to amplification of DNA segments which do not include the polymorphism.

Claims 2-11 depend from claim 1, but do not clarify the issue.

9. Claims 36-44 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Claim 36 is drawn to a method for determining the presence or absence of *M. tuberculosis* in clinical material comprising: (a) extracting microbial DNA from clinical material.

The omitted steps are: 1) differentially extracting microbial DNA from DNA which is not microbial in origin, but is from the host subject.

Claims 37-44 and 51 are dependent claims, but do not correct the deficiency in steps.

10. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites "wherein one probe in the probe pair comprises SEQ ID NO:4 and the other probe SEQ ID NO:5 or one probe in the probe pair comprises the complementary sequence of SEQ ID NO:4 and the other probe the complementary sequence of SEQ ID NO:5. It is unclear if "the other probe" consists of SEQ ID NO:5 or comprises SEQ ID NO:5. It is also unclear if "the other probe the complementaly sequence" comprises SEQ ID NO:5 or consists of SEQ ID NO:5.

11. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites "wherein one probe in the probe pair comprises SEQ ID NO:4 and the other probe SEQ ID NO:6 or one probe in the probe pair comprises the complementary sequence of SEQ ID NO:4 and the other probe the complementary sequence of SEQ ID NO:6. It is unclear if "the other probe" consists of SEQ ID NO:6 or comprises SEQ ID NO:6. It is also unclear if "the other probe the complementary sequence" comprises SEQ ID NO:6 or consists of SEQ ID NO:6.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 28 is rejected under 35 U.S.C. 102(b) as being anticipated by Fleischmann et al (U.S. Pat. No. 6,294,328, 25September2001).

The claim is drawn to a hybridization probe. The only requirement is that it be a sequence comprising SEQ ID NO:6 or the complementary sequence thereof.

Fleischmann et al teach one sequence (SEQ ID NO:1) which comprises instant SEQ ID NO:6 at residues 1287095-1287113 and a second sequence (SEQ ID NO:2) which comprises instant SEQ ID NO:6 at residues 1286564-1286582.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Wednesday from 9:00 AM to 7:30 PM EST. Thursday is the examiner's work at home day.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's Supervisor, Robert B. Mondesi (571)272-0956.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rodney P. Swartz, Ph.D./

Primary Examiner, Art Unit 1645

October 27, 2008